Defined electrical stimulation emphasizing excitability for the development and testing of engineered skeletal muscle.

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Public Summary:
Electrical stimulation is required for the maturation of skeletal muscle and as a way to nondestructively monitor muscle development. However, the wrong stimulation parameters can result in electrochemical damage that impairs muscle development/regeneration. The goal of the current study was to determine what aspect of an electrical impulse, specifically the pulse amplitude or pulse width, was detrimental to engineered muscle function and subsequently how engineered muscle responded to continuous electrical stimulation for 24 h. Acute stimulation at a pulse amplitude greater than six-times rheobase resulted in a 2.4-fold increase in the half-relaxation time (32.3±0.49 ms vs. 77.4±4.35 ms; $p<0.05$) and a 1.59-fold increase in fatigability (38.2%±3.61% vs. 60.6%±4.52%; $p<0.05$). No negative effects were observed when the pulse energy was increased by lengthening the pulse width, indicating electrochemical damage was due to electric fields at or above six-times rheobase. Continuous stimulation for 24 h at electric fields greater than 0.5 V/mm consistently resulted in ~2.5-fold increase in force (0.30±0.04 kN/m^2 vs. 0.67±0.06 kN/m^2; $p<0.05$). Forty per cent of this increase in force was dependent on the mammalian target of rapamycin (RAP) complex 1 (mTORC1), as RAP prevented this portion of the increase in force (CON=0.30±0.04 kN/m^2 to 0.67±0.06 kN/m^2 compared with RAP=0.21±0.01 kN/m^2 to 0.37±0.04 kN/m^2; $p<0.05$). Since there was no increase in myosin heavy chain, the remaining increase in force over the 24 h of stimulation is likely due to cytoskeletal rearrangement. These data indicate that electrochemical damage occurs in muscle at a voltage field greater than six-times rheobase and therefore optimal muscle stimulation should be performed using lower electric fields (two- to four-times rheobase).

Scientific Abstract:
Electrical stimulation is required for the maturation of skeletal muscle and as a way to nondestructively monitor muscle development. However, the wrong stimulation parameters can result in electrochemical damage that impairs muscle development/regeneration. The goal of the current study was to determine what aspect of an electrical impulse, specifically the pulse amplitude or pulse width, was detrimental to engineered muscle function and subsequently how engineered muscle responded to continuous electrical stimulation for 24 h. Acute stimulation at a pulse amplitude greater than six-times rheobase resulted in a 2.4-fold increase in the half-relaxation time (32.3+/-0.49 ms vs. 77.4+/-4.35 ms; $p<0.05$) and a 1.59-fold increase in fatigability (38.2%+/-3.61% vs. 60.6%+/-4.52%; $p<0.05$). No negative effects were observed when the pulse energy was increased by lengthening the pulse width, indicating electrochemical damage was due to electric fields at or above six-times rheobase. Continuous stimulation for 24 h at electric fields greater than 0.5 V/mm consistently resulted in approximately 2.5-fold increase in force (0.30+/-0.04 kN/m(2) vs. 0.67+/-0.06 kN/m(2); $p<0.05$). Forty per cent of this increase in force was dependent on the mammalian target of rapamycin (RAP) complex 1 (mTORC1), as RAP prevented this portion of the increase in force (CON=0.30+/-0.04 kN/m(2) to 0.67+/-0.06 kN/m(2) compared with RAP=0.21+/-0.01 kN/m(2) to 0.37+/-0.04 kN/m(2); $p<0.05$). Since there was no increase in myosin heavy chain, the remaining increase in force over the 24 h of stimulation is likely due to cytoskeletal rearrangement. These data indicate that electrochemical damage occurs in muscle at a voltage field greater than six-times rheobase and therefore optimal muscle stimulation should be performed using lower electric fields (two- to four-times rheobase).